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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,992	03/15/2004	Gary J. Beck	D-2804CON2	2049

7590 06/02/2008  
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EXAMINER
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JAGOE, DONNA A

ART UNIT	PAPER NUMBER
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1614

MAIL DATE	DELIVERY MODE
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06/02/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/800,992	<b>Applicant(s)</b> BECK ET AL.	
	<b>Examiner</b> Donna Jagoe	<b>Art Unit</b> 1614	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 February 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 31-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 31-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/12/08</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicants' arguments filed February 12, 2008 have been fully considered and they are deemed to be persuasive regarding previous rejections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

However, upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

#### ***Claims 31-50 are pending in this application.***

Claims 31-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lofftson U.S. Patent No. 5,472,954, Remington's Pharmaceutical Sciences (U) and Lipari U.S. Patent No. 4,383,992 and further in view of Dziabo et al. U.S. Patent No. 5,424,078.

Lofftson et al. teach an ophthalmic composition (column 18, lines 8-12) comprising a cyclodextrin, such as the sulfobutyl ether of  $\beta$  cyclodextrin (column 6, line 60) and an anti-inflammatory steroid (column 19, lines 16-39), such as prednisolone (see table 10, column 28). The ophthalmic cyclodextrin composition has water added in addition to the active ingredient along with pH adjusters, buffers and preservatives, in a sterile isotonic buffered aqueous solution (column 19, lines 24-31).

Lofftson et al. does not teach the acetate salt of prednisolone.

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Lofftson et al. teach that cyclodextrins are capable of forming inclusion complexes with a wide variety of hydrophobic molecules by taking up a whole molecule or some part of it into the cavity (column 2, lines 5-8). Lofftson et al. describes the solubilizing effects of cyclodextrins. Although Lofftson et al. does not specifically describe prednisolone acetate, one would have been motivated to employ prednisolone acetate in the cyclodextrin ophthalmic solution of Lofftson et al. motivated by the teaching of Lipari below and by the teaching of Remington's Pharmaceutical Sciences who teaches that prednisolone is slightly soluble in water but prednisolone acetate is practically insoluble in water. It would have been made obvious to one of ordinary skill in art at the time it was made to employ prednisolone acetate in the ophthalmic composition of Lofftson et al. Such a modification would have been motivated by the reasoned expectation of producing an ophthalmic composition that will be solubilized in an aqueous solution and which has enhanced effectiveness due to the complexation with the cyclodextrin carrier for comprehensively treating persons suffering from ophthalmic afflictions. In holding an invention obvious in view of a combination of references, there must be some suggestion, motivation or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in the way that would produce the claimed invention. This motivation may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. Here, filtered through the nature of the problem to be solved, the prior art (Remington's Pharmaceutical Sciences) disclosed that prednisolone acetate is practically insoluble in water, and that this problem can be

addressed by employing the known solubilizing agent, cyclodextrin or sulfobutylether  $\beta$  cyclodextrin, and a preservative as taught by Lofftson et al.. Accordingly, there was clear motivation to combine the prednisolone acetate and cyclodextrin derivatives with a preservative agent in an aqueous ophthalmic composition.

Lipari teaches an ophthalmic liquid composition comprising prednisolone acetate (column 1, lines 20-24) and a cyclodextrin derivative,  $\beta$  cyclodextrin (see abstract), in a solution (column 1, line 59 to column 1, line 6). The composition increases partitioning of the steroid compound into the cornea with an increased therapeutic response (column 3, lines 65-68).

Lipari lacks a teaching of a preservative and it does not teach an ophthalmically acceptable tonicity level, pH and buffer.

Dziabo et al. teach an ophthalmic composition preserved with a stabilized chlorine dioxide preservative with an ophthalmically acceptable tonicity component and a buffer to maintain the pH of the ophthalmic formulation within the physiological range (see abstract). It would have been obvious to one of ordinary skill in the art at the time it was made to employ chloride dioxide as a preservative in an ophthalmic preparation motivated by the teaching of Dziabo et al. who employs stabilized chlorine dioxide as a preservative for ophthalmic preparations and teaches that ophthalmic preparations must have ophthalmically acceptable tonicity and buffer to maintain the pH of the ophthalmic formulation within the physiological range and Lipari who teaches that prednisolone acetate is made soluble for ophthalmic use by employing  $\beta$  cyclodextrins. The method of preserving ophthalmic agents was recognized as part of the ordinary capabilities of

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one skilled in the art. One of ordinary skill in the art would have been capable of applying this known technique to a known composition that was ready for improvement and the results would have been predictable to one of ordinary skill in the art. The gap between the Lipari's ophthalmic composition of prednisolone acetate and cyclodextrin preserved with Dziabo et al.'s ophthalmic preservation system and the instant invention is simply not so great as to render the composition and method of use nonobvious to one reasonably skilled in the art.

It would have been made obvious to one of ordinary skill in art at the time it was made to employ chloride dioxide as a preservative in an ophthalmic preparation motivated by the teaching of Dziabo et al who employs stabilized chlorine dioxide as a preservative and acceptable tonicity and buffers to maintain the pH for ophthalmic preparations.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

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be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 31-50 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,358,935. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires an active therapeutic agent in combination with a cyclodextrin and a preservative wherein the preservative is stabilized chlorine dioxide or sorbic acid. The portion of the patent that supports conflicting claims 1-18 teaches that the active agents include prednisolone acetate (column 6, line 10). Instant claims 31-50 would be encompassed by the conflicting claims. It would have been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Claims 31-50 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,723,353. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and conflicting claims recite substantially the same

subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires an active therapeutic agent in combination with a cyclodextrin and a preservative wherein the preservative is stabilized chlorine dioxide. The portion of the patent that supports conflicting claims 1-13 teaches that the active agents include prednisolone acetate (column 6, line 11). Instant claims 31-50 would be encompassed by the conflicting claims. It would have been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

### ***Response to Arguments***

Applicant asserts that Lipari is silent with respect to preservatives or sulfur-containing derivatives of  $\beta$  cyclodextrin and neither Lipari nor Dziabo discuss or disclose the particular problems associated with formulating a preservative in a cyclodextrin-containing solution and neither reference discloses or suggests sulfur containing  $\beta$  cyclodextrin derivatives. In response, in holding an invention obvious in view of a combination of references, there must be some suggestion, motivation or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in the way that would produce the claimed invention. This motivation may flow from the prior art references themselves, the knowledge of

one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. Here, filtered through the nature of the problem to be solved, the prior art (Remington's Pharmaceutical Sciences) disclosed that prednisolone acetate is practically insoluble in water, and that this problem can be addressed by employing the known solubilizing agent, cyclodextrin or sulfobutylether  $\beta$  cyclodextrin, and a preservative as taught by Lofftson et al. Preservatives for ophthalmic agents, such as stabilized chlorine dioxide and sorbate derivatives are well known in the art as recited in Dziabo et al. Accordingly, there was clear motivation to combine the prednisolone acetate and cyclodextrin derivatives with a preservative agent, such as stabilized chlorine dioxide or sorbate derivatives in an aqueous ophthalmic composition.

Applicant has indicated that U.S. Patent No. 5,985,310 is provided in an IDS to provide evidence that cyclodextrin containing compositions are not easily preserved with, e.g. chlorobutanol, methylparaben and propylparaben. In response, The Examiner directs Applicant's attention to *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned.

They are part of the literature of the art, relevant for all they contain." A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Further, *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d

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1213, 1215 (Fed. Cir. 2005)(reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component); *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. “The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed.”) Consequently, this argument does not raise an issue of material fact.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./  
Examiner  
Art Unit 1614

May 22, 2008

/Ardin Marschel/  
Supervisory Patent Examiner, Art Unit 1614